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## Minutes

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Concerning:	<b>Development Committee Meeting, Basel 21 November 2002</b>	

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### **Summary of Main Points**

- **Thiamethoxam in rice:** progress in the main market Japan has been slow due to rapidly changes in conditions. Efforts are now focused on seedling box application with a novel TMX+pyroquilon formulation, and on the in-water segment with a granule formulation.
- **NOA 446 510:** the project is on track. Early market entry remains a critical success factor and efforts are made to initiate the chronic rat study early in 2003. The reasons for the poor performance in some grape trials can be attributed to the presence of resistant strains; detailed work has shown this risk to be small in the main target market (control of *Phytophthora* in potato).
- **Novel Inerts:** performance-modifying 'inerts' are expected to assume greater importance in future. A discussion took place on whether Syngenta should develop synthetic chemistry competence in this field to reduce the dependence on external suppliers.
- **Gramoxone image projects:** globally, there are 51 projects in this area. The need for strong management commitment and effective knowledge management was recognised.
- **Azoxystrobin Allergen project:** the project has been promoted to Stage B. About USD 50 Mio of additional business is expected, but since we are entering a new market there are also substantial risks. First sales are expected in 2005. **During 1-2Q 2003 demonstration of product performance and benefits are critical for project progression**
- **Mesotrione USA – rotational cropping:** the copper salt of mesotrione is up to 3x as persistent as the acid. Appropriate measures are in place, but a residual risk of some damage to the following crops on up to 1% of the treated area remains.

### **1. Minutes of the last meeting**

Item 5 – Product Stewardship: Participants reiterated the need for better coordination and transparency of the various activities taking place in Syngenta in areas such as the Food Chain, Sustainable Agriculture, Issue Management and Product Stewardship. It was also felt important to maintain awareness of Regional initiatives and to ensure alignment with corporate programmes or even integration when appropriate. Unequivocal ownership and funding of activities in these fields is a further aspect that requires attention.

There was agreement that activities agreed had high priority.

### **2. Feed-back from the CPMT Portfolio Review**

V. Anthony summarised the outcome of the discussions in Miami.

Projects saving approx. \$ 18 Mio in work for HAES have been identified. About half of this relates to a delay in the promotion to Stage 3 of SYN 449 280, the rest represents contributions from projects and tasks across all Product Lines. A number of options considered were rejected since the savings were small in relation to the size of business lost.

HAES have now also released the staff-day rates that will apply for 2003. Since they had to be increased significantly compared to this year, the gap in work requests and available capacity in HAES is closing only very slowly.

L. Smith reminded the group that the problem was not basically one of HAES not being able to do the work, but rather of the Development budget not being sufficient to cover the cost.

Further efforts to achieve a balanced work slate for next year continue.

### 3. Thiamethoxam – the Asia rice project

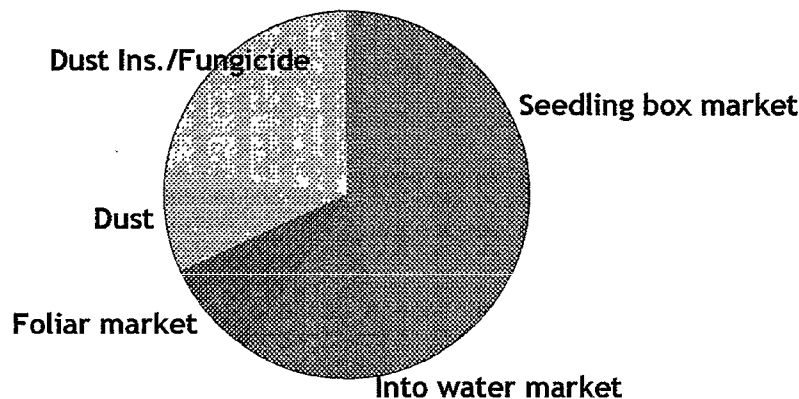
The topic was presented by R. Senn and P. Camblin.

Considerable efforts have been made in recent years to establish thiamethoxam in rice, particularly in Japan, the largest and potentially most lucrative market.

A number of changes in the market have thwarted the original strategies and necessitated a fundamental shift in our approach:

- The crop protection market in rice is shrinking and the bearable prices are declining.
- There has been a change in pest spectrum in Japan from hoppers to stinkbug
- More applications are made to the seedling box at the expense of foliar and into water applications in the field. This change has largely been driven by the introduction of new products.

The Japanese rice insecticide market is worth approximately \$ 350 Mio of which 45% is represented by the seedling box segment.



#### Currently existing Thiamethoxam solutions

- Actara Foliar application WG25/SG10: sold in India, SE Asia, China, Taiwan, Korea, Colombia; in Japan this has low priority given the small (aerial) segment where liquids can be used.
- Actara GR1: sold in Korea for in-water application
- Thiamethoxam GR2: registered in Japan in 2001 for seedling box use; not sold for lack of competitiveness.
- BION/Actara (2 formulations): Seedling box  
Korea: stopped  
Japan: registered in Oct. 2002; sales will start in 2003 and continue until about 2006 when acibenzolar stocks will be exhausted. There may also be some competition from newer, more profitable products for formulation capacity.
- Digital thiamethoxam/pyroquilon: Seedling box application; registered in 2002 with first sales planned for 2003

#### Strategy and outlook for thiamethoxam in rice

- Enter seedling box market with the first product
- Differentiate vs. competitors through fungicide mixing partner and formulation technology innovation
- Pursue opportunity to control stink bug
- Supply tech. AI for foliar market segments

Seedling box

Product	Crop	Country & Reg. Date	2003 Dvt costs (\$'000)	Sales Impact	Remarks/Goals/Priority
<b>TMX+Az+pyroquilon</b> (4+6+4)	Rice SB (I/F: long lasting)	Japan 2007	0	\$ 14 mio	Low stinkbug activity, no release of AZ >> no further development work: on hold for the time being.
<b>TMX + pyroquilon</b> (2+12)	Rice SB (I/F)	Japan Sold by Zennoh exclusively	361	\$ 18.3 mio	Get formulation cost down (\$ 8 -> \$2): shift to pan coated formulation in 04, old formulation sold in 03; HIGHEST PRIORITY

The TMX+ pyroquilon product provides season long control and is fully supported by Zennoh. There is some concern about possible phytotoxicity effects with pyroquilon in late transplanting in Southern Japan. The pan-coated formulation will be more cost-effective. Further testing will be required for confirmation of the release behaviour and the crop safety. The two-way mixture TMX plus AZ is on hold and no development costs are forecasted for 03.

Into water

Product	Crop	Country & Reg. date	2003 Dvt costs (\$'000)	Sales Impact	Remarks/Goals
<b>GR 0.5</b> (60kg/ha)	Rice: stinkbug at heading	Japan Registered in 2004	212	No sales planned	Fast registration with existing vegetable formulation, but 2 x price of current standard
<b>GR3</b> (10kg/ha)	Rice: stinkbug at heading	Japan Replace GR 0.5 in 2005		5 Mio	Will replace 0.5GR; target market North Japan because of target species

The GR 3 formulation will enable growers to replace aerial spraying with a convenient in-water application.

Sales will be limited to the northern Japan, since only 2 of the occurring species of stink bug are controlled well. With this spectrum it may difficult to achieve the desired differentiation from other products and combination with pyroquilon will be considered to achieve this.

Additional projects

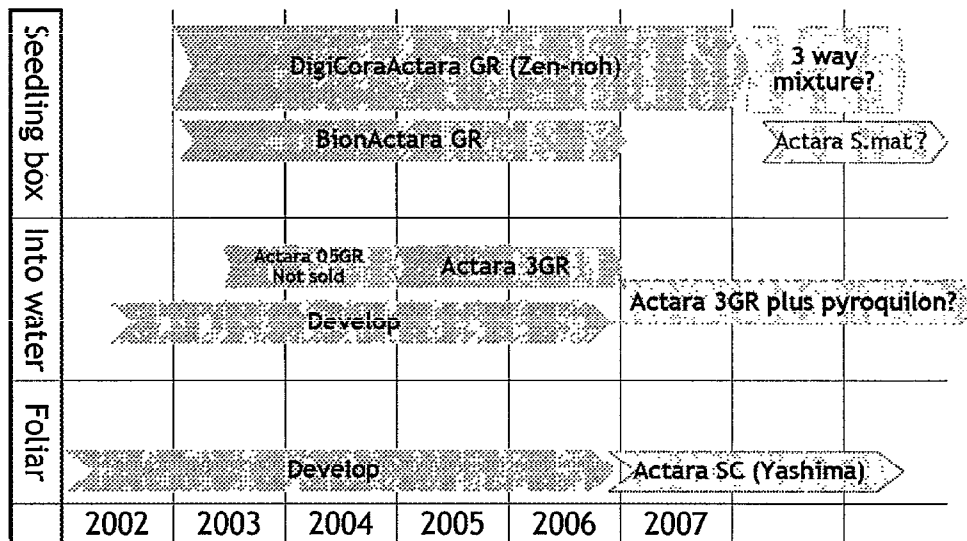
A number of projects are pursued and (mainly) funded by local distributors:

- Seedling mat impregnation: Collaboration with Korean 3rd party. Possibility of patent protection. The efficacy is still insufficient due to leaching and further improvements are required.
- Actara SC240: Late aerial stinkbug application. 3rd party Yashima project; sales of technical AI only; the final goal is a pre-mixture with AZ.
- MC100 Microcapsules: Seedling box spray for northern Japan; Daiichi formulation; persistence needs improvement.

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Exhibit 069 Page 4

Thiamethoxam life cycle management in rice:**Discussion and conclusions**

Considerable effort and investments have been made in Japan and yet tangible results have been somewhat elusive.

The launch of Digital Actara in 2003 for seedling box use provides the first entry for thiamethoxam into this important segment. It is important that the phyto risk is managed carefully in order not damage the reputation ahead of the change to a more cost-effective and safer formulation. It was pointed out to the team that it was Syngenta policy to focus on fewer formulations than in the past, and to make certain that promised objectives were achieved. In practice this will mean that projects will have to be planned more carefully and that factors such as the likely development of the market, the regulatory environment or competitor activity would have to be considered carefully and factored into the strategy and project plans. Formulations that are developed and registered should normally lead to profitable sales and not to 'shelf' registrations. Whenever possible, technically and commercially adequate formulations should be launched right from the start and not merely as expensive and technically marginal placeholders for follow-up products. Doubts were also expressed, whether pyroquilon was the right partner product for thiamethoxam for in-water application as a granule, since inferior performance could easily tarnish the image of thiamethoxam.

- 3.1. Action: Consider whether pyroquilon is a suitable partner to thiamethoxam for in-water application. R. Senn
- 3.2. Action: Maintain awareness of Japanese formulation projects, ensure they are well linked to local, Regional and global commercial aspirations and that that agreed projects are managed professionally. P. Camblin



#### 4. Project Review: NOA 446 510

The project was presented by Messrs Huggenberger, Cottrell, Gisi, Schneider, Theurig, Oostendorp, Weichsel and Gutmann. K. Gehmann participated in the review.

Aspects related to product safety will be reviewed at the DeCo of December 13.

Introducing the topic, F. Huggenberger confirmed that good progress had been made in general and that in particular considerable insight had been gained into the likely risk from resistance to AMS fungicides. The project was on track and the technical and commercial attractiveness of the project remained unchanged. Speed to the market remained a critical success factor and an early start of the long term toxicity studies had high priority.

#### Field development (F. Huggenberger)

##### Introduction, basic technical properties

SYN 446510 is active against foliar *Oomycete* pathogens, there is no activity against *Pythium* spp. The mode of action is currently unknown, but probably single site inhibition and probably identical to iprovalicarb, benthiavalicarb.

There is an immediate stop of fungal growth due to a strong effect on zoospore germination, growth restriction on mycelium, inhibition of haustoria formation and a reduced number of sporangiophores per sporulation point.

Uptake and translocation through the leaf with some translaminar activity. Leaf uptake can be enhanced through the addition of surfactant. There is little/no root uptake, little/no acropetal or basipetal translocation. There is good rainfastness after drying of deposit (1 hour after treatment). Degradation of surface deposit on the leaves appears to be relatively rapid and weekly spray intervals may be optimal under conditions of high disease pressure.

Excellent fruit protection has been observed, possibly because of good stability of the deposit in the wax layers of fruit.

The activity is mainly preventive and very little curative activity can be expected.

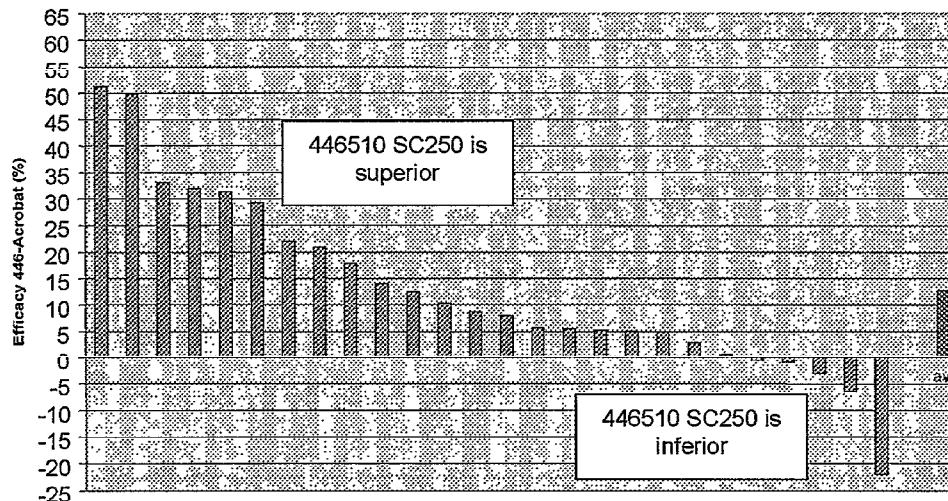
The substance is strongly adsorbed to soil particles, biological availability in soil is low and no promising results with soil applications or seed treatment should be expected.

##### SC250 against *Phytophthora infestans* in potatoes:

446510 SC250 at 100-150 g AI/ha is very effective against late blight in potatoes. It is more effective than current (dimethomorph, cymoxanil, famoxadone, fenamidone) or future (cyazofamid, mixtures based on iprovalicarb, benthiavalicarb) competitors.

The efficacy of 446510 is less reliable at application rates below 100 g AI/ha and there is no efficacy advantage when increasing application rates above 150 g AI/ha. Under high disease pressure, the product needs to be applied at spray intervals of between 7 and 10 days. High adjuvant concentration appears to enhance the efficacy.

Typical results of field trials during 2002: comparison 100g AI/ha with Acrobat M at 180 g AI dimethomorph+1200 g AI mancozeb/ha:



#### 446510+metalaxyl-m against *Phytophthora infestans* in potatoes:

At 100+80 to 125+100 is very effective against late blight in potatoes and it is clearly better than metalaxyl-m+mancozeb at 100+1600 g AI/ha. Compared to 446510 alone there is a clear advantage of the mixture in some of the trials

#### 446510+mancozeb against *Phytophthora infestans* in potatoes:

At 100+1200 to 125+1500 is clearly better than mancozeb alone at 1200-2400 or dimethomorph+mancozeb at 180+1200 g AI/ha. Compared to 446510 alone at 100-125 g AI/ha there is a clear advantage of the mixture in some of the trials.

#### Disease Control in Vegetables

446510 is generally more effective than current (dimethomorph, cymoxanil, famoxadone, fenamidone) and future competitors (cyazofamid, mixtures based on iprovalicarb, benthiavalicarb). The product is generally more effective at spray intervals of 7 days than at 10-14 days and it should be recommended as preventive treatment.

In brassicas and in onions / leeks 446510 should be recommended in tank mix application with an adjuvant (spray oil, silicon wetter, nonionic surfactant).

Combination products are of interest to complement the efficacy of 446510 as follows:

- Metalaxyl-m for added curative activity (10-15 g AI/hl)
- Azoxystrobin metalaxyl-m for added curative activity for extension of spectrum (10+8 to 12.5+10 g AI/hl)
- Chlorothalonil for increase in persistence, extension of spectrum, resistance management (10+15 to 12.5+18.75 g AI/hl)

Vegetables represent a fragmented market with different requirements and it may be difficult to justify the development of products specifically for vegetables except for tomatoes / cucurbits.

#### Control of *Plasmopara viticola* in grapes

At 15 g AI/hl is effective against downy mildew in grapes except at Marsillargues (FR), Les Barges (CH) and Estillac (FR). At these sites resistant strains have been selected through intensive, season-long use of AMS-compounds for four seasons.

446510 generally provides excellent disease control on bunches in comparison with treatments based on dimethomorph and mancozeb. There are indications that late leaf infections at least 3 weeks after last spray are not well controlled, possibly indicating a relatively short persistence of the compound on/in leaves.

In combination, mancozeb at 150-240 g AI/hl was clearly more effective than dithianon at 42-105 g AI/hl, but in sensitive situations 446510 was clearly able to contribute to the performance of mancozeb.

#### Comparison with benthiavalicarb

- Rate for rate 446510 is better than benthiavalicarb against *Phytophthora infestans* in potatoes
- 446510 is comparable to benthiavalicarb against *Plasmopara viticola* in grapes
- 446510 is comparable to benthiavalicarb against *Phytophthora infestans* in tomatoes
- 446510 is weaker than benthiavalicarb against *Pseudoperonospora cubensis* in cucumbers

Benthiavalicarb has been observed in a number of markets in mixture chlorothalonil, pyraclostrobin, mancozeb and folpet. A single formulation included in official trials in Japan since 1998 is not likely to be commercialised.

#### **AMS Resistance Risk Assessment** (H.U. Gisin)

Resistant isolates were found in three Syngenta experimental vineyards (2 FR, 1 CH) following season-long use of AMS-compounds for three seasons for the control of *Plasmopara viticola*. This explained the clearly unsatisfactory field performance at these sites in 2002. Recent data have proven there is **cross resistance to iprovalicarb and benthiavalicarb, as well as unexpected dual- or cross resistance to dimethomorph in isolates of *Plasmopara viticola***. No cross resistance with other known fungicide classes has been observed.

No resistant isolates of *Phytophthora infestans* were found in

- greenhouse selection experiments (tuber slices; discontinuous epidemic)
- a polytunnel experiment (continuous epidemic; up to 11 treatments)
- under field conditions (leaf samples collected from 17 sites)

#### Preliminary conclusions for resistance risk

At present, the resistance risk is estimated as low to medium for *P. infestans*, medium to high for *P. viticola* and unknown for other related pathogens (*Peronospora*, *Pseudoperonospora*, *Bremia*,...)

In potatoes, AMS may be used in spray programmes as a single product.

In vines mixtures between AMS and MLX or AZ will not be an adequate anti-resistance strategy. Instead, block treatments with the three chemistries (multisite contact fungicides) should be considered.

It should also be assumed that a maximum 1/3 of sprays applied in a programme should be treatments including an AMS-compound.

#### **Product Concepts** (A. Cottrell)

The main targets are:

- Late Blight in potatoes and tomatoes
- Downy mildew in Cucurbits
- Downy mildew in grapes

First sales are planned from 2006 (Asia), 2007 (USA, Switzerland) and 2008 (most European markets). The PLT now needs to define what it is they want to intend to sell.

The target for the end of this year is to

- Put 446 on the agenda of key country marketing contacts
- Define 446 product proposition for each key market



- Update the 446 business plan
- Ensure key countries prepare „milestones to launch“ plan
- Monitor competitor activities

Current sales projections:

At plateau (\$m) 2011/ 2012; full allocation and lead AI concept; confirmed with regions.

Crop / Region	Potatoes	Grapes	Vegetables	Total (mio \$)
EUA	42	25	8	75
NAFTA	12	-	11	23
LAT	7	-	3	10
AP	10	3	11	24
<b>Total</b>	<b>71</b>	<b>28</b>	<b>33</b>	<b>132</b>

Detailed business plans are in preparation in key countries. Early indications are that sales predictions will broadly be confirmed. A number of assumptions have changed since the promotion to Stage 3 one year ago:

- AZ mix not for grapes in Europe
- Increased interest in solo formulation for potatoes and vegetables
- Need for a multisite contact fungicides mix in grapes

Pillars of AI positioning:

New chemistry: Mandelamide  
 Powerful protection: Top efficacy; adsorbed in wax layer; translaminar;  
 Reliably better: Good persistence; curative; rainfast  
 Safe: To the crop, environment, user and consumer

Product Concept Solo:

Strengths	Weaknesses
<ul style="list-style-type: none"> <li>- Flexibility – rate, timing, partner</li> <li>- Lower risk of cannibalisation</li> <li>- No dilution of AI benefits</li> <li>- Cost effective</li> </ul>	<ul style="list-style-type: none"> <li>- Single site MOA</li> <li>- Narrow spectrum</li> <li>- Limited curativity</li> <li>- No systemicity</li> </ul>
Opportunities	Threats
<ul style="list-style-type: none"> <li>- Develop clear identity</li> <li>- Maximization of Syngenta share</li> <li>- Full exploitation of AI benefits</li> <li>- Food chain linkage</li> </ul>	<ul style="list-style-type: none"> <li>- Dev. of resistance</li> <li>- Poor perceptions due to other diseases remaining in crop</li> <li>- Poor results due to incorrect timing and/or application</li> </ul>

Product Concept with mefonoxam

Strengths	Weaknesses
<ul style="list-style-type: none"><li>- Premium Oomycetes control</li><li>- Consistent performance</li><li>- Curative and systemic</li><li>- Margin</li></ul>	<ul style="list-style-type: none"><li>- Single site MOAs</li><li>- Narrow spectrum</li><li>- Spray number restrictions</li><li>- Negative phenylamide perceptions</li></ul>
Opportunities	Threats
<ul style="list-style-type: none"><li>- Defend MFX volumes</li><li>- Brand leadership in potatoes</li><li>- Food chain linkage</li></ul>	<ul style="list-style-type: none"><li>- Development of dual resistance</li><li>- Poor perceptions due to other diseases remaining in crop</li><li>- Poor results due to MFX resistance</li><li>- Business defence, but no growth</li></ul>

Product Concept azoxystrobin

Strengths	Weaknesses
<ul style="list-style-type: none"><li>- Premium oomycetes control</li><li>- Leverage of azoxystrobin</li><li>- Margin</li><li>- Onion DM</li></ul>	<ul style="list-style-type: none"><li>- Single site mode of actions</li><li>- Spray number restrictions</li><li>- Negative strobilurin perceptions</li><li>- Cost</li></ul>
Opportunities	Threats
<ul style="list-style-type: none"><li>- Defend AZ volumes</li><li>- Exploit all market segments</li><li>- Food chain linkage</li></ul>	<ul style="list-style-type: none"><li>- Development of dual resistance</li><li>- Restriction to high value niches</li><li>- Poor results due to AZ resistance</li><li>- Business defense, but no growth</li></ul>

Product Concept Contact

Strengths	Weaknesses
<ul style="list-style-type: none"><li>- Anti-resistance option</li><li>- Spectrum</li><li>- Cost-effectiveness</li><li>- Limited cannibalisation</li></ul>	<ul style="list-style-type: none"><li>- Negative profiles of partner options</li><li>- Restricted crop range</li><li>- No curativity</li><li>- No systemicity</li></ul>
Opportunities	Threats
<ul style="list-style-type: none"><li>- Maximisation of 446 life-cycle</li><li>- Exploit all market segments</li><li>- Maximisation of Syngenta share</li></ul>	<ul style="list-style-type: none"><li>- 446 HSE benefits negated</li><li>- Multiple options required to cover all markets</li><li>- Poor results due to incorrect timing and/or application</li></ul>

In order to guide development, our understanding of product choice drivers will need to improve. Some global market research in combination with local knowledge will be essential to shape our product proposition, but other AMS products will to some extent define the playing field. We will need to monitor competitor activity very carefully, collect performance reports and intelligence on marketing and promotion activities for Iprovalicarb and the development approach and timelines that emerge for benthiavalicarb.

Iprovalicarb, the first AMS fungicide has just been launched mainly for use in grapes. It is too early to judge its performance, but it is not thought to be outstanding. The new information on cross-resistance to dimethomorph means that a detailed understanding of market use, selection pressure and intelligence on fungal insensitivity to this product is now an imperative.

**Process development and production plan** (H.D. Schneider)

The project milestones are as follows:

<b>Milestones</b>	<b>planned</b>
• Process fix	Q4 / 2004
• 5 Typical batches	Q2 / 2005
• Base Set intermediates, notification	2005
• First formulation frozen	Q1 / 2003
• Product Chemistry	10/2005
• Plant introduction first formulation	2006
• Plant introduction intermediates, A.I.'s	2006
• First sales	2006/7

Achievements so far:

- 125 kg NOA446510 were delivered mid of March for Formulation and Field Dev.
- 250 kg NOA446510 were analysed under GLP and released as tox-batch by end of March
- S-enantiomer SYN 504213 has been produced, but the project has now been terminated
- Brainstorming sessions held at all PT sites with the support of research; an extensive synthesis catalogue has been prepared and costs of raw materials are being collected
- Process development will be an international effort with teams at EZA, Huddersfield and Cold Creek pooling their know-how

Objectives:

Provide formulation development and biology with sufficient active ingredient by end February 2003 to support the 2003 field programme.

**Formulation development** (S. Gutmann)

Solo formulation (SC 250 with 22% adjuvant)

The lead formulation is on track. The chemical stability does not pose any problems and the phys.-chem. stability after 6 months storage at 35 °C is still satisfactory.

Freezing in February 2003.

Combi with mefenoxam (SC 125/100 with 20% or 22% adjuvant)

There is limited data available on chemical stability, but this is unlikely to be an issue.

Phys.-chem. stability after 1-month storage at 50 °C looks promising, particularly the variant containing 20% adjuvant.

Long-term storage stability data is outstanding, but information will be available to support freezing in August 2003.

**Combi with chlorothalonil** (SC 040/400 or, as 2. priority, WG 4/40)

Chem. stability: No data but unlikely to be an issue.

The SC is a simple blend of standard CTN formulation with AMS millbase and no significant problems with phys.-chem. stability are expected.

The initial properties of the WG are promising, however it is too early for storage data to be available.

Optimisation of stabilizer resp. dispersing system is in progress. The planned freezing date is February 2004.

**Combi with mancozeb** (WG 5/60 - Fluid bed dried granules including adjuvants)

Only preliminary data exist at present. Freezing scheduled for Feb. 2004.

**Combi with azoxystrobin** (SC 250/375)

Chem. stability: No data but unlikely to be an issue; phys.-chem. stability after 8 weeks storage at 40 °C is satisfactory. Some processing problems caused by high solid content have been solved on the lab scale. The use of azoxystrobin millbase as starting material is not possible because of the high formulation strength.

The required freezing date is still open and the demand for the formulation needs to be confirmed.

**Product safety** (M. Theurig)

To cover all possible uses, metabolism studies in 3 different crop categories are done: grapes, potato and, next year, lettuce. There is some concern that we may not have done enough work in the field to understand what parameters should be used in the lettuce study. Crop metabolism indicates parent only as residue of concern.

Relatively high TTR in wheat grain need to be watched and studied further.

Results from animal metabolism studies indicate that there is no accumulation in milk and fat – good news.

Higher tier studies for non-target arthropods yield favourable results, indicating that the AI should be suitable for use in IPM programmes.

The intrinsic toxicity to earthworms is fairly high, but at present not of concern where only a single crop is grown and treated. The risk needs to be assessed for situations where sequential crops are treated several times each during the year. This seems particularly relevant, since the DT<sub>50</sub> can be up to 80 days and the DT<sub>90</sub> up to 390 days.

More work will be done, but it is obvious already that the soil/environment will be a key part of the ai profile that will require specific management.

**Intellectual property** (C. Weichsel)

No third party patent rights have emerged so far and Syngenta should therefore be free to make, use and sell NOA 446510.

The European Patent Office has confirmed this evaluation by issuing a very positive International Preliminary Examination Report on our published patent application WO 01/87822.

Following the EPO's conclusions on patentability, no major problems or obstacles should occur during patent prosecution: smooth granting of patent rights is expected in the designated countries, more than 70 world-wide.

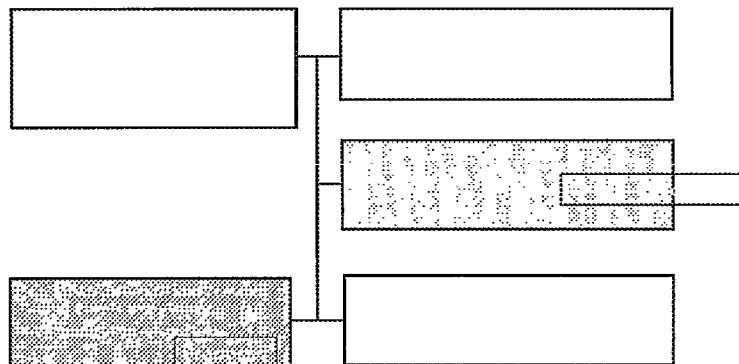
Syngenta should also be free to adopt the intended production process in the main production countries.

Though less likely with time passing, in the USA a "submarine patent" application by AgrEvo may still be pending, corresponding to WO 94/29267. Regular checks will continue, even though we may never get certainty about the fate of the hypothetical US application in case AgrEvo have abandoned it like all other corresponding patent applications of that patent family.

The patent situation of sales mixtures and formulations for NOA 446510 needs to be checked, once the final decision is taken on feasible sales combinations. Likewise, if the final production process deviates from the intended variants, re-confirmation of the patent situation is required.

### Development plan (M. Oostendorp)

The project is now structured as follows:



All major milestones remain as originally proposed. The start of the 2-year chronic study has been delayed to await results of an Investigative Tox programme. Also not time-critical studies in Ecotox, Ecochemistry and metabolism have been re-scheduled to start in late 2003 and 2004. The expected development spent has increased from \$ 37 Mio to \$ 45.8.

#### Major increases:

- New cost estimate for field development and residues trials: \$ 4.5 Mio
- Investigative Toxicology program: \$ 1.5 Mio
- Additional US soil ecochemistry study needs: \$ 1.2 Mio
- Process Technology analytical cost: \$ 0.5 Mio
- New Contact-Mix formulation: \$ 0.7 Mio

#### Activities on the critical path:

- Start of 2-year chronic tox study - January 2003
- Freezing of Solo Formulation for residue trials – Q1 2003
- Residue trials for solo formulation in 2003 and 2004 seasons
- Freezing of mixture formulations – before 2004 season
- Relevant metabolites known – Q4 2003

### Discussion and conclusion

Good progress is visible and recognised.

The clear understanding of the poor performance in some of the vine trials removes a major uncertainty and provides clear guidance for the development strategy. Phytophthora control in potato now clearly represents the most valuable target, followed by the vegetable segment. The solo formulation may often be the best approach in potato, but decisions may vary market by market, depending on the level of discipline and adherence to recommendations that exist. Vine remains important, but given the challenges in this segment, the team will need to ensure that the resources allocated to the segment are commensurate with the expected contribution.

Resistance management needs to be an important consideration in selecting mixing partners and in defining future use programmes.

Given the relatively clear understanding that now exists, it should be possible to select the formulations that will be developed as soon as possible and to stop investing on the others. Science will no doubt continue to provide further insight into the mode of action and the mechanism involved in the development of resistance, but this information is not expected to be available in



time to help with the initial development strategy. Work in this field should be done in-house whenever possible to prevent premature dissemination of awareness about cross resistance to dimethomorph.

It is very important to agree expected use programmes early. In particular the total number of applications and the pre-harvest intervals that are envisaged under practical use should be defined before relevant metabolism and residue studies are initiated. Apart from aspects related to performance and the management of resistance, the needs of the food chain and for import tolerances should also be considered in detail at that stage.

Given the profile of the molecule, to claim 'curative' action seems questionable. Also there appears now to be enough information available to discount any uses as a soil applied fungicide or for seed treatment uses. Not only does the compound lack the requisite mobility, it also lacks activity against some main targets such as *Pythium*.

Formulation work is well on track and combi formulations do not appear to pose particular challenges thanks to the considerable experience that exists with most likely partner compounds. Current formulations do not include any adjuvants/inerts that are likely to be restricted in future. The need for early tox testing will be considered case by case.

- 4.1. Action: Select formulations as early as possible and stop investment in others. F. Huggenberger
- 4.2. Define the need for import tolerances; involve regulatory and commercial staff in the regions establish a detailed plan. M. Theurig/M. Oostendorp
- 4.3. Up-date knowledge on the regulatory status of mancozeb and other multi-site protectant partners should be sought for all relevant markets. M. Theurig/DeCo 13.12.02.
- 4.4. Plan strategy for information release and communication consistent with publication of patents, registration of common name, etc. F. Huggenberger
- 4.5. Consider any special needs of the food chain; discuss and agree with M. Gut-Rella. F. Huggenberger
- 4.6. Further evaluation for soil application or use in seed treatment does not appear to be warranted. J. Yoder
- 4.7. The International Design Documents should be up-dated to the prescribed format. F. Huggenberger/DeCo 13.12.02.
- 4.8. Detailed analysis of market penetration, use and intelligence on product performance of dimethomorph to be sought and used as part of defining the anti-resistance strategy for NOA 446510. A Cottrell/F Huggenberger/ U Gisi

## 5. Novel Inerts Strategy

The topic was presented by D. Stock, supported by B. Brown and D. Saddler.

The main objectives of investing in novel inerts are to

- Maintaining a technical advantage for off-patent products
- Reduce the rate of application (cost effectiveness)
- Reduce non-target losses (environmental & operator safety)
- Provide regulatory & consumer advantages
- Build obstacles to generic competition

- Obtain patent protection on enhanced-performance offerings

Some examples of this approach already exist in Syngenta, e.g. APG patents with glyphosate, Turbocharge technology, Atlox 4913 dispersant, use of phosphonate adjuvants (Bayer patent).

So far we have probably purchased about 80% of our needs from external, specialised suppliers of adjuvants. For a further 10 % we have worked with partners and in the remaining cases we have found solutions in-house.

With 4-5 % of the production going to the agchem industry we are relatively minor customers for the manufacturers of adjuvants. They have, however, realised how important some of these materials are to us and to what extent they add value to what we sell. As a consequence, they endeavour to protect their property more effectively so that they can retain a larger part of the value specific adjuvants represent.

Research-based agchem companies and manufacturers of inerts have somewhat different core competencies:

Syngenta	Inert Manufacturers (Uniqema, Cognis, Rhodia)
<ul style="list-style-type: none"> <li>• <b>Regulatory expertise</b></li> <li>• <b>Formulating into acceptable systems</b> (robustness)</li> <li>• <b>Screening for efficacy</b></li> <li>• <b>Design of adjuvants</b> (using modelling &amp; SAR analysis)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Inert design</b> (functional inerts – dispersants etc)</li> <li>• <b>Manufacture</b></li> <li>• Some regulatory expertise</li> </ul>

There appears to be little overlap in key areas and as it would be costly for manufacturers of inerts to establish the biological and regulatory capabilities that exist in major agchem companies, it would probably also be difficult to compete with the manufactures in the design of functional inerts. Regulatory skills in particular could be critical if new materials have to be registered with EPA.

Viewed from a Syngenta perspective a SWOT analysis indicates the following situation:

	Strength	Weakness	Opportunity	Threat
<b>Buy</b>	No up-front costs.  Should be closer to market.	Poor IP position  Waiting for something useful!	Could gain leverage on supplier by regulatory support	Technology offered to competitor
<b>Joint</b>	Reduces direct costs to Syngenta	Will need to give something away.  Time to reach agreement.  Time to market	Access to the manufacture capability of key suppliers	How good is the agreement? Can something similar be offered to competitor?
<b>In House</b>	Full control of process Full IP control	Requires significant cash input.  Time to market.  Competing with our suppliers	Broad IP claim, limiting competitor & generics.  Potential to out-license?	Finding route to market; may not be able to toll (could depend upon a key supplier)

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Based on the detailed analysis the team concluded that there was no single best model. The best approach is likely to depend upon chemistry, regional issues, volumes etc. The decision issues are largely similar to make/buy decisions involved in commercial manufacture of a new active ingredient. Another consideration is of course where we believe R-dollars are best spent. The team feels that in some cases this could be in finding the best possible inert rather than a new molecule. They envisage that at some point in future up to 40% of the inerts we use could come from internal developments.

Specific in-house developments would appear to be particularly meaningful in the case of

- Defence of a Blockbuster product
- Broad application across the portfolio for enhanced technical performance, e.g. reactive polymeric surfactants for surface modification
- Broad application across portfolio for enhanced bio-performance e.g. adjuvant systems for enhanced uptake of lipophilic active ingredients

The proposed strategy is

- Review current portfolio to determine products at risk based upon current inerts and establish product replacement options and timelines.
- Develop a list of specific areas where novel inerts could add value (defence and expanding into new markets)
- Modify existing product development processes and relationships to minimize the impact of identified hurdles

### Discussion and conclusions:

DeCo agrees with the team in their assessment of the importance of inerts/adjuvants as a potential competitive advantage in future. There is less unanimity in how best to exploit opportunities that may present themselves. There was in particular concern that a team of between 5 and 10 FTEs to work in this field (as envisaged by the proponents) would be 'unaffordable and yet too little' at the time.

Although cost was one factor to consider, it was also felt that the discussion should focus on the benefits that could be created.

There was a strong view that we should not endeavour to compete with the manufactures of inerts in their area of core competence, but that we should do enough to put ourselves in a favourable position to work with them. This meant that we should have a number of knowledgeable people in this field in Syngenta, that we should maintain a relationship with key players – existing suppliers and others – and that we should enter into collaborative agreements, whenever this was called for. Part of our skill-set would also be to negotiate favourable agreements that gave us maximum commercial leverage over any intellectual property involved and relevant to our area of activity.

- 5.1. Action: R & T should continue to take the lead in designing concepts for progression of Novel Inerts and submit them for joint review to R&T, D and T&P. D. Sadler;B. Brown

### 6. Gramoxone Image Projects & Stewardship Update

The topic was presented by J. Barnes, D. Scott and M. Voerman.

Image projects are defined as those concerned with economic, environmental or social aspects of Gramoxone use on a Global or Regional scale to improve the product image. All projects have an element of stewardship.

Projects are generally designed with the output in mind and managed to ensure results are delivered. Key items that are considered are:

- Who's the audience
- What's the message
- Key learnings
- How will it be used versus stakeholders
- How will the impact be measured

The number of projects are:

Region	Projects	Main type of projects
APAC	21	Training, soil erosion, medical survey, industrial weed mgmt.
LATAM	10	No-till, Human safety, training, soil erosion, biodiversity
EAME	6	Soil health, soil erosion, literature search
NAFTA	4	Weed resistance/shift, training
Global	10	Human safety, treatment, training, suicide prevention, worker exp.

A number of key projects were described:

Title	Objectives
Product Stewardship in China	<ul style="list-style-type: none"> <li>• Ensure key stakeholders have the proper attitude to Gramoxone - Aim at broad coverage and downstream post WTO acceptance</li> <li>• Demonstrate agronomic benefits and fit to sustainable agriculture</li> <li>• Enhance product image - Value added programs to business growth</li> <li>• Responsible and safe use of agricultural products through training – strengthen the preventive approach against any likely issues/risks</li> </ul>
Farmer Training in Vietnam	Develop Guidelines for Safe & Effective Use of Pesticides in combination with AG PPS ( Our Distributor in VN), and the Plant Protection Authority (PPD)
Chronic Effects Health Study in Vietnam	<ul style="list-style-type: none"> <li>• Address concerns that paraquat poses a health risk to farmers</li> <li>• Convince the MOH that the use of paraquat will not cause health problems in farm workers</li> <li>• Provide Data needed to support de-restriction</li> </ul>
Health Survey of Paraquat-Exposed Workers in Costa Rica	<ul style="list-style-type: none"> <li>• To compare the respiratory health of paraquat-exposed plantation workers with those who have not worked with the product</li> <li>• To measure paraquat exposure in a subset of workers using biomonitoring in order to calculate their long-term exposure</li> <li>• To increase confidence that paraquat is safe in normal occupational use.</li> </ul>
Gramoxone European Soil and Water Conservation Projects	<ul style="list-style-type: none"> <li>• To develop of approaches and technologies for soil and water conservation in annual and perennial crops in Europe</li> <li>• A tool for influencing key stake holders</li> <li>• To develop Syngenta crop solutions, with Gramoxone as a key driver</li> <li>• To Demonstrate the benefits of Gramoxone in the Environment</li> </ul>

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The current hotspots are:

Location	Issue	Response
Switzerland	- Erklärung von Bern/NGO) - food company challenge	Engagement - Persistent / engaged - Neutral/positive
Malaysia	Notice of de-registration	User group lobbying - Pesticide board meeting
France	Safe use esp. knapsack	Academic CdeToxic bias - Due process re-established
Dominican Republic	Drift incident	Alerting agent drift - Team there now
Western Samoa	Suicide issues	Co-operation with global and local suicide prevention groups
Sri Lanka	Suicides	Benchmark study - Prometheus
Costa Rica	- Central America focus - Health study	POPs challenge - Submission made - reporting early 2003

### Discussion and conclusions

DeCo was impressed to hear that there are a total of 51 Gramoxone/pq image/stewardship projects running, but some members also expressed the wish to understand the more fully, how these projects were chosen, initiated and then managed.

Although the objectives of the effort were generally understood and supported, there was some concern about whether messages were always delivered in the most appropriate and locally accepted way. J. Barnes provided assurances that qualified local personnel were always involved and ultimately responsible for the communication platform chosen.

The results of the campaign were often difficult to assess, but efforts were made to measure effects whenever possible. The commitment of local management was still an issue in some cases, but was seen as a critical success factor.

Surprisingly, the consistency of label information across geographies is still not at the expected level and further efforts are required to achieve a standard that will not offer a target to our critics. Views on how visible our efforts in support of safe use of Gramoxone and to improve its image varied among decision makers, depending on the particular situation in a market. There was agreement that this was an aspect that required very careful thought and a well defined strategy. The motives of some of those involved was clearly not governed by generally recognised drivers nor were they interested in scientific arguments.

- 6.1. Action: To aid understanding across all of Syngenta (HQ, region, countries, functions) provide a clear outline of governance of paraquat stewardship activities, together with all planned or ongoing image projects. This should include key information such as project sponsor/owner/manager, objectives, costs, timelines and deliverables. J. Barnes



## 7. Azoxystrobin Allergen Project: Promotion to Stage B

The topic was presented by D. Meier and J. Tweedy from NAFTA and J. Yoder and M. Wilks; G. Dickson participated by phone.

The project had started as a collaboration with Medachieve – a group formed in 1986-87 with a focus on a preventative program for asthma and allergies. In 2002 the Syngenta testing agreement with Medachieve expires and will not be renewed by Syngenta for commercial reasons.

It is thought that there are 15 mio Americans with asthma and 30 mio suffering from allergies. Sufferers are increasing 5% per year and the average cost for treatment is estimated at \$ 3,260 per patient and year. More than \$ 800 Mio per year is spent on over-the-counter medications. The anti-allergen market is projected to be a \$ 1000 Mio non-pharmaceutical business by 2010. This will include air filters, mattress encasements, duct cleaning and cleaning solutions (i.e. Acarosan).

The business cases assumes net sales (\$ '000) as follows:

2005	2006	2007	2008	2009
7,123	24,151	39,055	45,350	51,676

### Project Concept:

- Application of permethrin + Azoxystrobin; preventative component of a disease management program
- Professional application to carpets and other soft textiles, post-manufacture
- Product is applied after thorough professional cleaning
- Applied through professional, trained and certified carpet cleaners

### Stage B Development Strategy

- Develop a pre-mix of perm + Az:
  - Must be equal or better than existing products
  - Must meet all exposure and residential safety criteria
  - Target for fixed formulation: Sept. 2003
- Formulation testing
  - Carpet integrity
  - Interaction with carpet components and additives (stain and soil blockers)
  - Interaction with cleaning equipment
  - Evaluate application technology
- Submit for IP protection (US & ROW)
- HAES program continues in support of project
- Biology: evaluate efficacy against house dust mite and mold and duration of control
- Regulatory
  - Conduct appropriate regulatory studies and final label
  - HAES studies (frozen formulation)

### Develop certification programme for carpet cleaners

- Develop a stewardship programme
- Design a marketing and launch programme

The formulation must meet a number of important criteria:

- Must have a 'Caution' Label
- "Hypoallergenic" (or close to it)
- Clear/light in colour
- Minimal odour
- Must adhere to fibers
- Minimally affected by water quality
- Easy to use and clean out of equipment
- No negative effects on carpet wear
- Compatible with anti-stain/soiling products
- Quick drying

Biological profiles:

Permethrin – house dust mite	
Strength	Concerns
<ul style="list-style-type: none"><li>- Control of American &amp; European HDM</li><li>- Established insecticide throughout world; used in medical field</li><li>- Acceptable tox profile</li><li>- Cost effective with favorable cost position</li><li>- Reduction in HDM strongly correlated with reduction of Der f1 allergens</li></ul>	<ul style="list-style-type: none"><li>- Resistance management required</li><li>- Percent mortality of females versus males, nymphs and larvae</li><li>- Sensitive population targeted for use - chemophobia</li><li>- Non-proprietary product</li><li>- Permethrin EPA RED</li></ul>
Azoxystrobin – molds	
Strength	Concerns
<ul style="list-style-type: none"><li>- Az has broad spectrum activity against targeted fungi</li><li>- FDL available for resistance strategy</li><li>- Favorable tox profile</li><li>- Excellent cost position and gross margin</li><li>- Proprietary products; Components for IP protection</li><li>- Length of control not as critical as HDM; primary activity needed during carpet drying phase (72 hrs.)</li></ul>	<ul style="list-style-type: none"><li>- Final rate not confirmed for fungal control in carpets</li><li>- Resistance management required</li><li>- Life cycle of pathogens in carpeting needs to be determined</li><li>- Some fungi are producers of potent human allergens; limits internal ability to do testing</li><li>- Bayer and BASF have similar chemistries</li></ul>

Risk assessment:

A carpet transfer study provided a positive HAES assessment; the final formulation will be needed for final assessment. Margins of exposure of 100 or less would not be acceptable to EPA.

Scenario	Adult Margin of Exposure	Child Margin of Exposure
Azoxystrobin: Indoor treatment	6800	3900
Permethrin: Indoor treatment	700	350

Litigation risk – higher in residential market than agricultural market; consequences:

- As with usual practice efficacy claims must be supported with data , otherwise we are vulnerable to fraud claim
- Adequate & appropriate human safety and exposure tests must be conducted

Routes to reduce liability:

- Product applied by certified professional applicators
- Limit use to carpets - putting on mattress will increase liability

Active safety stewardship program:

- Gain support from medical professionals, activist groups, carpet professionals
- Certify applicators
- Provide environmentally responsible disposal method for any excess spray solution
- Educational programs - eliminate or minimize biases
- Positive media placement for product

US regulatory strategy:

#### Azoxystrobin

- Add molds to the Heritage master label
- Prepare directions for use as a carpet anti-microbial
- Model on existing products in market
- Meet with EPA anti-microbial division
- Timeframe to new registration 9-12 months (4Q03)

#### Permethrin

- Add house dust mite as target pest to current Prelude label (3Q03)
- Mid-term worst-case scenario for cost of defence to Syngenta ~ \$ 2 Mio
- Defend RED (collaboration with HAES)
- Join other registrants to support active
- Support evaluation of possible permethrin alternatives

#### Final Product Registration:

- Novel (aqueous suspo-emulsion) formulation of Perm + Az
- Earliest submission 1Q04

Competitive products:

Brand	Active ingredient	Manufacturer	What It Controls	Comments
Acarosan	Benzyl Benzoate	Bissel	House Dust Mites	Short duration of control; compliance
Mite-Nix	Benzyl Benzoate	Gemtek	House Dust Mites	Short duration of control; compliance
Aller-RX	Non-ionic surfactant	Easy Breathin'	House Dust Mites	Limited efficacy; compliance
Allersearch X-mite or AllerDust	Tannic Acid	Allersearch	House Dust Mites Molds	Can stain carpet, hard to apply
Dustmitex	Borate	Ecological Works	House Dust Mites	Short duration; hard to apply, compliance
Aveho (animal allergen control)	Borate	AVEHO	House Dust Mites	Short duration; hard to apply, compliance
Dustroy	Natural occurring rock & extracts from plant	Safe Care	House Dust Mites	Short duration; limited information
Smite (WP & EC)	Permethrin	Medachieve via Aventis	House Dust Mites	Poor formulation and lack of marketer
MagiSeal DM	Permethrin	MagiSeal?	House Dust Mites	Limited marketing; not in US?
Unisept	Phosphoric acid	Interface	Anti-microbial	Spectrum; lack of marketer

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Development investment:

Investment	2002	2003	2004
Formulation	\$64,303	\$664,524	\$543,354
HAES	\$89,719	\$304,881	\$645,373
Biology	\$75,000	\$570,000	\$300,000
Registration	\$2,000	\$5,000	\$10,000
<b>Total</b>	<b>\$231,022</b>	<b>\$1,544,405</b>	<b>\$1,498,727</b>

## Discussion and conclusions

The project is attractive because it will be entirely new business. It is also challenging, because we enter an unfamiliar new market with a new business model. The scope of the project is deliberately restricted to the treatment of carpets through professional applicators. The Deco supported and reinforced that the project should be limited to only exploration of use on carpets at this stage

- Treating carpets during production is less attractive, since dust mites are only considered a problem after use.
- Mattresses, settees, curtains, etc. are an important source of dust mites, but the treatment is deemed to be difficult. Incorporation into a washing powder may be an option for later.
- Distribution through D.I.Y channels would be attractive, but again only considered for a later phase.
- It would be attractive to be able to claim positive health effects, but this is considered too difficult to attempt at least during the initial phase; only control of dust mite and mold will be claimed.

There is concern that potential customers might feel uneasy about having a 'pesticide' applied to their carpets, particularly in situations where small children and pets are in frequent contact with them.

The project team has already worked with relevant focus groups and established that treatments as proposed would basically be accepted.

Permethrin may have to undergo cumulative risk assessment and it at present it is not clear, how this would affect the regulatory position. Alternatives are not available and it may prudent to evaluate some options. This is not only as potential alternatives to permethrin, but also to understand what competition from established players could appear if the market develops. It would help, if it was possible to protect some of the intellectual property involved in our approach.

Given that carpets are not the only harbouring place for dust mites, there was some concern that the rationale for the treatment we will offer could be undermined rather easily and that the market could then be much smaller than assumed. The Deco noted that there is only limited mold control data and that this is an important part of determining the product positioning and benefits. Emphasis must be put on understanding the performance properties of the mixture. Fungal combined with mite control is potentially the key differentiating feature from existing products and must be addressed in depth over the next 6 months. It was also highlighted that allergenicity testing should be done on the final scaled up formulation, which may require some revision of the timelines

- 7.1. Action: consider options for protecting intellectual property. J. Yoder; D. Meier/asap.
- 7.2. Action: evaluate what other substances could potentially be developed and used for the control of dust mite, e.g. tau-fluvalinate. D. Meier
- 7.3. Clarify the role of the ethics committee in a project like this and consider, if appropriate, when they should review the project. L. Smith/DeCo 13.12.02
- 7.4. DeCo supports the promotion of the project to Stage B with the scope to control house dust mite and mold on carpets. Work programme and expenditure is subject to inclusion in the Project Portfolio 2003. Particular emphasis on gaining more mold control data and performance of the fung/insecticide mixture is a key part of the external evaluation programme. J. Yoder; D. Meier
- 7.5. Timing of the allergenicity, human exposure studies to be re-explored with reference to when the final scaled-up fully representative formulation composition will be ready. D. Meier; D. Schabacker
- 7.6. A further review of the project should take place during Q2 2003. J. Yoder

### **8. Mesotrione USA – rotational cropping**

The topic was presented by D. Cornes and J. Garrett.

Mesotrione is formulated as the acid in CALLISTO. As the acid form is not stable in mixture with S-metolachlor, mesotrione is formulated as a copper salt in LUMAX and CAMIX, to achieve formulation stability. Initial laboratory studies indicated that once the mesotrione copper salt is in the soil, dissociation is rapid, after which it behaves like the acid with respect to degradation. These studies were carried out in moist soil, and under these conditions, the copper salt behaves like the acid. Because of this, all rotational recommendations on the initial LUMAX and CAMIX labels were based on trial work carried out with the acid. However, it has recently been discovered that this acid = copper salt assumption does not appear to hold true in all instances, especially where dry conditions follow application (see Deco minutes Sept 2002).

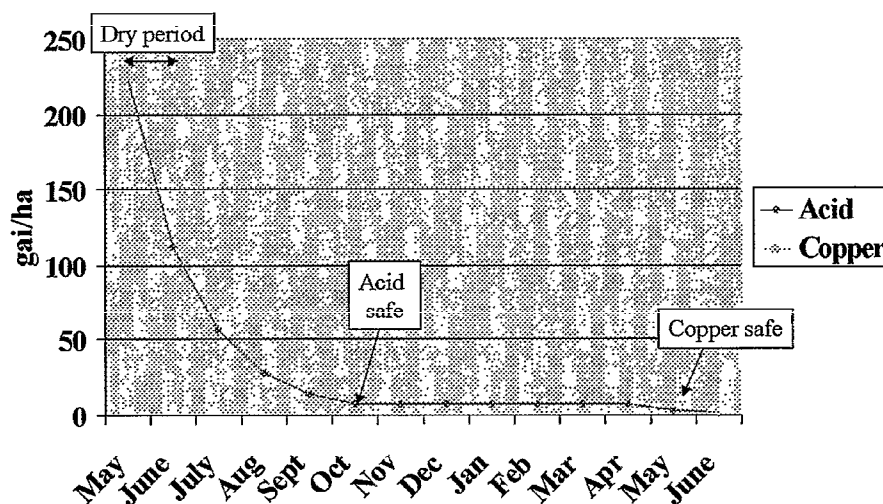
The rate of mesotrione in LUMAX and CAMIX is higher (~2x) than in CALLISTO, but the application timing is much earlier as well, thus more than compensating for the higher mesotrione rate in a typical setting.

Copper Salt vs Acid – Depiction of Assumed Degradation Differences Under Dry Conditions Following Application:

Analysis of soil samples from 24 field trials where the copper salt and acid have been directly compared (figure 3) shows that the copper salt was more persistent than the acid in ~20% of the cases, with up to 3x the amount of residue remaining. Many (but not all) trials showing differences had a dry period around application. On the fields where 3x residue remains, this means that an extra 1½ half-life periods will be required for degradation of the copper salt to acid levels



under these conditions.



Mesotrione degradation in dry conditions assuming 1 month (30 day) half life and no degradation over winter

The factors which increase or decrease the carryover risk of mesotrione are listed in the following table:

Increases Risk	Decreases Risk
Copper salt of mesotrione	Mesotrione acid
Late application (Post-em)	Pre-plant /Pre-em application
Low pH	High pH
Dry conditions (esp. around application)	Good moisture
Cool conditions, especially winter (Northern geographies)	Warm conditions, especially winter (Southern geographies)
Sensitive soybean varieties	Tolerant soybean varieties
Highly visible symptoms if carryover occurs (Bleaching)	Soybean shallow dose response curve and good recovery from early injury in soybeans
High rate	Low rates
Early soybean planting, in following season	Late soybean planting, in following season

#### Proactive Management Measures

- 1) *Restrict use in dry geographies (Western Minnesota, South Dakota, non-irrigated acres of Western Nebraska and Kansas).*  
Recommended. In these dry areas LUMAX will be positioned for use on irrigated areas. This is mainly due to LUMAX needing moisture for good efficacy and the fact that it will be too expensive for growers without irrigated yield potential.
- 2) *Restrict rotation based on an earlier "latest use" date. Change from June 10 to June 1.*  
Recommended. Will give a good risk reduction by removing late applications, which are the critical timing, owing to the increasing risk of dry weather conditions during June and the shorter re-planting interval.
- 3) *Open the pre-plant application window from 10 days to 14. This will encourage early applications by making pre-plant a more realistic opportunity.*  
Recommended. This should reduce risk but, probably, not by a large factor. (Note: field efficacy data exists to support this change).

- 4) *Restrict rotation based on a minimum rainfall following application:*  
Not recommended. No work has been done to define the minimum rainfall requirement and would be difficult to implement, plus this will flag up that we have a carry-over issue.
- 5) *Reduce maximum application rate from 3.0 qt/acre to 2.5 qt/acre.*  
Not recommended. LUMAX must be a one-pass solution and to succeed in delivering our objective, this requires 3.0 qt/acre on many soils.
- 6) *Change soybean replanting interval from "next spring" to 11 or 12 months. A move to a 12-month interval would come close to eliminating any risk*  
Not recommended. 11 months is unlikely to bring any benefit, as in practice the replanting interval is very rarely less than 11 months anyway. Any change to 11 months will flag up that we have an issue without bringing any benefit. 12 months is not commercially acceptable and would severely restrict the use potential, undermining the success of the product and the cornucopia strategy. It also implies that we have a major carryover issue, which is not the case.
- 7) *Using EDTA to dissociate (convert to the acid) mesotrione copper in the spray tank.*  
Only recommended, as a last resort if analysis in the next months shows our risk potential is higher than currently anticipated, as the practicality of implementation is questionable. Still needs to be proven biologically and logistically.

The recommended measures will be added to the product labels. Measure 1 will be implemented internally.

The measures are probably not enough to bring the risk of carry-over all the way to zero. The modified level of risk is probably in the 1% range or less, of treated area (which can increase if the season is very dry). This situation has been considered by the PLT and the NAFTA business and found to be an acceptable level of risk, given the importance of LUMAX to the corn strategy. We will need to identify any high-risk areas in advance of the 2004 planting season and be prepared to give pre-season management advice, in addition to being ready to handle any complaints.

Reactive Management Measures (if areas are deemed at risk of carry-over):

- 1) Very high risk. Recommend that the grower does not rotate to soybeans. This could occur significant cost and loss of image.
- 2) Moderate to high risk. Recommend one of the most tolerant soybean varieties (these still need to be characterised but should be feasible). Probably small cost but some loss of image.
- 3) Low to moderate risk. Recommend that the grower plants his LUMAX treated field last to give extra degradation period. Not significant cost.
- 4) Low risk. Allow to plant and handle any complaints. Any resulting carryover likely to be minor and low cost.

Replacement of Copper Salt in LUMAX and CAMIX

A project has been initiated to develop new formulations of LUMAX and CAMIX with either mesotrione acid (as in CALLISTO), a lower copper salt content (with some acid) or a different salt, which dissociates more readily. Other options under investigation include use of spray-tank additives other than EDTA.

If we are to replace the current LUMAX and CAMIX formulations for the 2004 season, these will need to be submitted to EPA by March 2003. To produce a new formulation in such a short time is very difficult, but this must be the goal. If this fails, we could only expect to introduce new versions of LUMAX and CAMIX for the 2005 season. This would mean that we would have to manage and mitigate the carryover issue for 2 seasons.

## Discussion and conclusions

Excellent progress has been made and the team was commended on the very thorough approach and the systematic plan.

Given the situation with Lumax and Camix it is important to ensure that the next formulations are thoroughly tested and represent sustainable solutions. The management measures appear comprehensive and given the discipline that prevails in the US market, and the commitment of our organisation, it can also be assumed that they will be implemented and will reduce the carry-over risk. There was some doubt whether growers would be willing to switch to new varieties of (more tolerant) soybeans. On the other hand, if they did follow the recommendation, we have to make certain that adequate supplies were available.

- 8.1. Action: The plan is supported; re-confirm that farmers would follow the recommendation to plant new varieties of soya and that supplies of seed would be available. D. Cornes

## 9. AI Development Activities (AIDA)

The topic was presented by R. Shaunak

The decision was taken at the DeCo of 5.12.2000 and confirmed on 20 June 2001 to produce brief monthly reports.

The reports were meant to

- provide an AI-based communication platform for all, but particularly remote, stakeholders in related projects and for line managers that were often not part of PLTs and project teams
- list highlights, important events and achievements concerning the projects and their environment
- to contain brief contributions (e.g. bullet points, e-mail style, one-liners, the odd pasted table or presentation, etc.)
- provide pointers to results and events that could have wider implications for a project so as to alert readers to pursue individually, if relevant.
- monthly, reliable, topical, up-to-date and interesting to read

The reports were **not** meant to

- be a comprehensive listing of all activities undertaken in a department or by individuals
- be in polished prose
- for core members of the PLTs
- take more time to write than 30-60 min per month and group leader

This has worked reasonably well for a while, but two issues have surfaced:

- With the migration to SAHARA, the templates used to compile the report appear to function less reliably and now often require time-consuming manual re-work
- Some authors still see it as a good opportunity to list all the work they have done during the months. Others find it difficult to think of any points that might be of interest to colleagues.

A survey conducted among all the authors and recipient has indicated that 70% of recipients find the report useful or very useful, but a majority recommended a quarterly, rather than a monthly report. Public folders (as usual) are not considered a convenient place to access the report and distribution by e-mail or via the Intranet are clearly preferred.

Based on the survey and the difficulties encountered with the reliability of the tool, the recommendation is made to continue with the report, but consider moving to a quarterly interval and also to spend \$ 20 Mio to develop a simple web application.

## Discussion and conclusions

DeCo continues to see value in sharing useful information we generate or gather within the development and CP community on a regular basis. The value of a quarterly report appears less obvious, given that information would usually be out of date. Also there seems to be a risk that the report would become even more voluminous than the monthly version – already considered to be too detailed by many.

- 9.1. Action: continue with the report on a monthly basis; re-issue a statement about the objectives and the guidelines about what should be included. A. Kohli
- 9.2. Action: fix the tool problem. If at all possible continue to use the current Word templates and only consider alternatives if all attempt fail. R.Shaunak/A. Stehli

## 10. Miscellaneous

### a) Thiamethoxam – ELISA method

The thiamethoxam Elisa kit development reached the point when it can be adopted as a new service tool for internal uses, such as complaint handling, training tool or as a sales support tool. There is also an opportunity to develop the same tool to identify thresholds for farmers after soil or seed treatment application.

Both PLTs (Actara and Cruiser) are recommending to develop full speed the internal uses and to evaluate in 2003 the potential for external uses.

Expenses in	2001	\$ 60'000
Estimated expenses:	2002	\$ 50'000
	2003	\$ 50'000
	2004	\$ 10'000

The price will be between 5 to 6 \$ per kit.

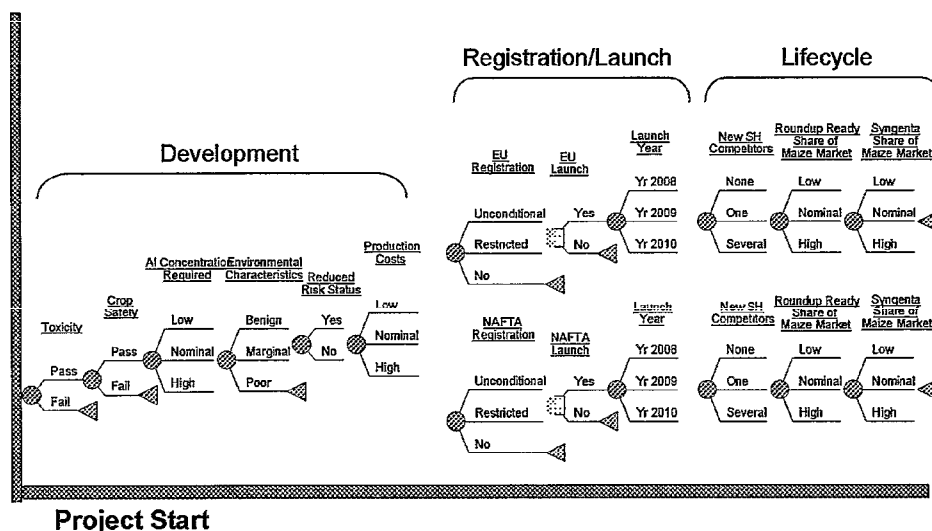
- 10.1. Action: DeCo supports the application of the method for in-house use. A review of the project by DeCo should be planned for Q1 2003. R. Senn; D. Hofer/26.3.03

### b) Real Option Analysis

Projects are very often evaluated, planned and implemented on the basis of a best/most realistic-case scenario. This approach does only take insufficient account of uncertainties such as opportunities and risks, particularly when a single discount factor is applied to all expenditure and income, independent of the risks involved.

Real Options Analysis is an approach that supports project managers in building a decision tree with milestones and options and that provides help in assessing volatility and risks so that different courses of action can be considered and compared.

Example of a simple decision tree:



Over 20 colleagues have recently attended introductory half-day seminar given by Dr. J. Mun, an expert and author in this field. 15 colleagues from development (incl. 1 each from NAFTA and EAME) and finance also participated in hands-on training workshop. It is planned to gradually apply the approach to a small number of suitable projects and to gain some experience.

### c) SYPOS II – NAFTA project

At the beginning of October the decision was taken to stop the development work on the original SYPOS project and to develop a new solution incorporating MS Project 2002.

During October NAFTA has now initiated under the local CSP2 a local project to finalize development of 4 modules of the original SYPOS project and to roll them out in NAFTA early next year.

Given the restricted resources that are available and the complexity added by an additional project drawing largely on the same resources, the global project manager has raised some concerns and suggested that the following points should continue to apply:

- The goal remains to build one global tool; the project team will focus on this objective.
- The SYPOS II project can only be charged by NAFTA for agreed services and actions; satellite activities to be funded locally.
- The global project has first call on resources within the agreed work programme.
- To the extent NAFTA staff are members of the global project team or providers of services, they will agree plans within the global project and not with NAFTA Management.
- NAFTA has strong representation on the global project team and NAFTA requirements have high priority. NAFTA needs to accept some compromises to enable a suitable global tool to emerge.

10.2. Action: DeCo wants to ensure that the implications need to be understood more fully and recommends that a discussion takes place at the SYPOS Steering Committee meeting of Dec. 13. Specific trade-offs and issues should be tabled then so that guiding decisions can be taken by the steering committee A. Kohli



**11. Actions**

- 3.1. Action: Consider whether pyroquilon is a suitable partner to thiamethoxam for in-water application. R. Senn 2
- 3.2. Action: Maintain awareness of Japanese formulation projects, ensure they are well linked to local, Regional and global commercial aspirations and that that agreed projects are managed professionally. P. Camblin 2
- 4. Project Review: NOA 446 510 2
- 4.1. Action: Select formulations as early as possible and stop investment in others. F. Huggenberger 2
- 4.2. Define the need for import tolerances; involve regulatory and commercial staff in the regions establish a detailed plan. M. Theurig/M. Oostendorp 2
- 4.3. Up-date knowledge on the regulatory status of mancozeb and other multi-site protectant partners should be sought for all relevant markets. M. Theurig/DeCo 13.12.02. 2
- 4.4. Plan strategy for information release and communication consistent with publication of patents, registration of common name, etc. F. Huggenberger 2
- 4.5. Consider any special needs of the food chain; discuss and agree with M. Gut-Rella. F. Huggenberger 2
- 4.6. Further evaluation for soil application or use in seed treatment does not appear to be warranted. J. Yoder 2
- 4.7. The International Design Documents should be up-dated to the prescribed format. F. Huggenberger/DeCo 13.12.02. 2
- 4.8. Detailed analysis of market penetration, use and intelligence on product performance of dimethomorph to be sought and used as part of defining the anti-resistance strategy for NOA 446510. A Cottrell/F Huggenberger/ U Gisi 2
- 5. Novel Inerts Strategy 2
- 5.1. Action: R & T should continue to take the lead in designing concepts for progression of Novel Inerts and submit them for joint review to R&T, D and T&P. D. Sadler;B. Brown 2
- 6. Gramoxone Image Projects & Stewardship Update 2
- 6.1. Action: To aid understanding across all of Syngenta (HQ, region, countries, functions) provide a clear outline of governance of paraquat stewardship activities, together with all planned or ongoing image projects,. This should include key information such as project sponsor/owner/manager, objectives, costs, timelines and deliverables. J. Barnes 2
- 7. Azoxystrobin Allergen Project: Promotion to Stage B 2
- 7.1. Action: consider options for protecting intellectual property. J. Yoder; D. Meier/asap. 2
- 7.2. Action: evaluate what other substances could potentially be developed and used for the control of dust mite, e.g. tau-fluvalinate. D. Meier 2
- 7.3. Clarify the role of the ethics committee in a project like this and consider, if appropriate, when they should review the project. L. Smith/DeCo 13.12.02 2
- 7.4. DeCo supports the promotion of the project to Stage B with the scope to control house dust mite and mold on carpets. Work programme and expenditure is subject to inclusion in the Project Portfolio 2003. Particular emphasis on gaining more mold control data and performance of the fung/insecticide mixture is a key part of the external evaluation programme. J. Yoder; D. Meier 2
- 7.5. Timing of the allergenicity, human exposure studies to be re-explored with reference to when the final scaled-up fully representative formulation composition will be ready. D. Meier;D Schabacker 2

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- 7.6. A further review of the project should take place during Q2 2003. J. Yoder 2
- 8. Mesotrione USA – rotational cropping 2
- 8.1. Action: The plan is supported; re-confirm that farmers would follow the recommendation to plant new varieties of soya and that supplies of seed would be available. D. Cornes 2
- 9. AI Development Activities (AIDA) 2
- 9.1. Action: continue with the report on a monthly basis; re-issue a statement about the objectives and the guidelines about what should be included. A. Kohli 2
- 9.2. Action: fix the tool problem. If at all possible continue to use the current Word templates and only consider alternatives if all attempt fail. R. Shaunak/A. Stehli 2
- 10. Miscellaneous 2
- a) Thiamethoxam – ELISA method 2
- 10.1. Action: DeCo supports the application of the method for in-house use. A review of the project by DeCo should be planned for Q1 2003. R. Senn; D. Hofer/26.3.03 2
- c) SYPOS II – NAFTA project 2
- 10.2. Action: DeCo wants to ensure that the implications need to be understood more fully and recommends that a discussion takes place at the SYPOS Steering Committee meeting of Dec. 13. Specific trade-offs and issues should be tabled then so that guiding decisions can be taken by the steering committee A. Kohli 2